## AMENDEMENTS TO THE CLAIMS

Claims 1-10 (Canceled)

Claim 11 (Withdrawn)

Claim 12 (Canceled)

Claim 13 (Withdrawn)

Claims 14-22 (Canceled)

Claims 23-24 (Withdrawn)

- 25. (New) A targeting construct capable of disrupting a PERK gene, the targeting construct comprising:
  - (a) a first polynucleotide sequence homologous to at least a first portion of a PERK gene;
  - (b) a second polynucleotide sequence homologous to at least a second portion of the PERK gene; and
  - (c) a selectable marker gene, located between the first and second polynucleotide sequences,

wherein the targeting construct produces a disruption in the PERK gene, wherein the disruption, when present in the genome of a transgenic mouse in a heterozygous state, results in one PERK gene allele which does not produce functional PERK protein and a phenotype of increased susceptibility to seizure, and when present in the genome of a transgenic mouse in a homozygous state, results in two PERK gene alleles which do not produce functional PERK protein and a phenotype of increased incidence of perinatal lethality.

- 26. (New) A method of producing a targeting construct capable of disrupting a PERK gene, the method comprising:
  - (a) providing a first polynucleotide sequence homologous to at least a first portion of a PERK gene;
  - (b) providing a second polynucleotide sequence homologous to at least a second portion of the PERK gene;
  - (c) providing a selectable marker gene, wherein the selectable marker gene is located between the first and second polynucleotide sequences; and
  - (d) inserting the first sequence, second sequence, and selectable marker gene into a vector, to produce the targeting construct,

wherein the targeting construct produces a disruption in the PERK gene, wherein the disruption, when present in the genome of a transgenic mouse in a heterozygous state, results in one PERK gene allele which does not produce functional PERK protein and a phenotype of increased susceptibility to seizure, and when present in the genome of a transgenic mouse in a homozygous state, results in two PERK gene alleles which do not produce functional PERK protein and a phenotype of increased incidence of perinatal lethality.

- 27. (New) A murine embryonic stem cell transformed with the targeting construct of claim 25.
- 28. (New) A transgenic mouse whose genome comprises a disruption in an endogenous PERK gene, wherein where the disruption is heterozygous, the transgenic mouse comprises one PERK gene allele which does not produce functional PERK protein and exhibits increased susceptibility to seizure.
- 29. (New) The transgenic mouse of claim 28, wherein the transgenic mouse exhibits seizure-like responses at a lower dose of metrazol, relative to a wild-type mouse.
- 30. (New) A cell or tissue isolated from the transgenic mouse of claim 28.
- 31. (New) A method of producing a transgenic mouse comprising a disruption in an endogenous PERK gene, the method comprising:
  - (a) introducing a targeting construct capable of disrupting the endogenous PERK gene into a mouse embryonic stem cell;
  - (b) introducing the mouse embryonic stem cell into a blastocyst;
  - (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
  - (d) breeding the chimeric mouse to produce the transgenic mouse comprising a disruption in the endogenous PERK gene,

wherein where the disruption is heterozygous, the transgenic mouse comprises one PERK gene allele which does not produce functional PERK protein, and exhibits increased susceptibility to seizure.

32. (New) A transgenic mouse whose genome comprises a disruption in an endogenous PERK gene, wherein where the disruption is heterozygous, the transgenic mouse comprises one PERK gene allele which does not produce functional PERK protein, and exhibits increased susceptibility to seizure, and wherein where the disruption is homozygous, the transgenic

- mouse lacks production of functional PERK protein and exhibits increased incidence of lethality during perinatal development.
- 33. (New) The transgenic mouse of claim 32, wherein the increased susceptibility to seizure is characterized by the transgenic mouse exhibiting seizure-like responses at a lower dose of metrazol, relative to a wild-type mouse.
- 34. (New) The transgenic mouse of claim 32, wherein the increased incidence of lethality during perinatal development is caused by a congenital abnormality.
- 35. (New) The transgenic mouse of 34, wherein the congenital abnormality comprises hydrocephaly.
- 36. (New) The transgenic mouse of claim 34, wherein the congenital abnormality is present in an organ selected from the group consisting of lung, heart, pancreatic gland, stomach and liver.
- 37. (New) A cell or tissue isolated from the transgenic mouse of claim 32.
- 38. (New) A method of producing a transgenic mouse comprising a disruption in an endogenous PERK gene, the method comprising:
  - (a) introducing a targeting construct capable of disrupting the endogenous PERK gene into a mouse embryonic stem cell;
  - (b) introducing the mouse embryonic stem cell into a blastocyst;
  - (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
  - (d) breeding the chimeric mouse to produce the transgenic mouse comprising a disruption in the endogenous PERK gene,

wherein where the disruption is heterozygous, the transgenic mouse comprises one PERK gene allele which does not produce functional PERK protein, and exhibits increased susceptibility to seizure, and wherein where the disruption is homozygous, the transgenic mouse lacks production of functional PERK protein and exhibits increased incidence of lethality during perinatal development

- 39. (New) A method of identifying an agent that modulates a phenotype associated with a disruption in a PERK gene, the method comprising:
  - (a) providing a transgenic mouse whose genome comprises a heterozygous disruption in the PERK gene, wherein the transgenic mouse comprises one PERK gene allele that does

not produce functional PERK protein and wherein the transgenic mouse exhibits increased susceptibility to seizure;

- (b) administering a putative agent to the transgenic mouse of step (a); and
- (c) determining whether the putative agent modulates the susceptibility of the transgenic mouse to seizure.